REMARKS

I. Claim Status

Claims 1-48 are pending. Claims 40 and 45 have been amended and claims 46-48 have been added by way of this response.

Claim 40 has been amended at the suggestion of the Examiner to incorporate Figure 2 directly into the claim. Support for this amendment is found in the specification at page 21, lines 30-31, and in Figure 2.

Claims 25 and 45 has been amended, without prejudice or disclaimer, to delete the terms "transmucosal system," and "transmucosal device."

Claims 46-48 have been added. Support for these claims is found throughout the specification, for example, at page 5, lines 19-26, page 8, lines 15-17, page 16, lines 25-28, and page 21, lines 17-29.

All amendments are supported by the application as originally filed. Accordingly, no new matter has been added by way of this Response.

II. Claim Rejections

The claim rejections set forth in the Office Action are summarized and addressed as follows.

(i) Rejections Under 35 U.S.C. § 112, second paragraph (indefiniteness).

The Examiner has rejected claim 40 for indefiniteness because the claim refers back to the specification for additional information. The Examiner asserts that the plasma profile presented in Figure 1 and referenced in the claim must be reproduced in the claim itself.

In response, Applicants respectfully submit that reference to Figure 1 in claim 40 was made in error, and that the plasma profile intended to be recited in the claim appears in Figure 2. Accordingly, claim 40 has been amended to incorporate the plasma profile of Figure 2 into the body of the claim. In view of this amendment, withdrawal of the indefiniteness rejection is requested.

The Examiner has rejected claim 45 for indefiniteness because it recites "transmucosal delivery" but depends from a claim that recites "transdermal delivery." Accordingly, the Examiner contends that dependent claim 45 is improper because these routes or administration are neither analogous, nor is either one a subset of the other.

Applicant notes that the specification does disclose that a transdermal dosage form can be a transmucosal system or a transmucosal device. However, in order to advance prosecution, claim 45 has been amended, without prejudice or disclaimer, to delete the terms "transmucosal system" and "transmucosal device." Thus, the Examiner's rejection to claim 45 is rendered moot and should be withdrawn.

(ii) Rejection under 35 U.S.C. § 103(a).

Claims 1-45 have been rejected as allegedly obvious over Hille. The Examiner asserts that Hille teaches a transdermal patch for 24 hour delivery of buprenorphine. Although Hille does not teach the re-administration of the buprenorphine patch, the Examiner contends that this would be routine advice that any doctor would give to chronically ill patients. The Examiner further states that the dosing methods of the present invention are nothing more than a description of a common pain management practice.

"In determining the differences between the prior art and the claims, the question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious, but whether

the claimed invention as a whole would have been obvious" (emphasis originally present). See, M.P.E.P. § 2131. Although the Examiner asserts that Hille teaches a transdermal buprenorphine patch and that it would be obvious to re-administer the Hille patch, the Examiner has failed to address why it would have been obvious to increase the dose of buprenorphine in the Hille patch upon re-administration. Even if the re-administration of a buprenorphine patch would have been obvious, the prior art does not teach or suggest increasing the buprenorphine dose according to the claimed regimen. Therefore, the obviousness rejection has not been properly applied to the claimed invention as a whole and is inappropriate.

Applicants further submit that the presently claimed methods are based on the discovery that, by administering a first, a second, and a third transdermal dosage form of buprenorphine, wherein the second dosage is equal or greater then the first, and the third dosage is greater than the second, adverse events are significantly reduced compared to administering equal dosages throughout treatment (*See* specification, page 7, lines 14-19). This reduction in adverse events is best illustrated in Example 6, wherein the incidence of nausea, vomiting, and headache were reduced by dose escalation (i.e., titration) of buprenorphine (to 20 mg over 6 days), as compared to direct administration of 20 mg of buprenorphine with repeated dosing over the same time period (i.e., routine re-administration). Consequently, the practice of the claimed methods, as opposed to the routine dosing schedule presented by the Examiner, improves overall patient compliance to a buprenorphine treatment regimen. The Examiner has provided no arguments evincing that the re-administration of the Hille buprenorphine dosage would reduce the adverse events typically associated with a routine buprenorphine dosage regimen. Furthermore, Hille does not teach or

suggest the reduction of adverse events that would result from the practice of the presently claimed invention. For this additional reason, claims 1-45 are not obvious over Hille.

For the foregoing reasons, Applicants respectfully submit that the section 103 rejection over Hille is traversed and should be withdrawn.

(iii) Provisional Obviousness-type Double Patenting Rejection

Claims 1-48 have been rejected for obviousness-type double patenting over claims 1-28 and 34-132 of U.S. Application No. 10/736,049. Applicants request that this rejection be held in abeyance until allowable subject matter has been identified.

CONCLUSION

In view of the above remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

By _____

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